BIOFUNCTIONAL MAGNETIC NANOPARTICLES FOR LABELLING STEM CELLS

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Biofunctional nanomaterials provide the potential for huge improvements in biomedical sciences including diagnosis, therapy and imaging. The use of stem cells to correct and regenerate some cell populations is being explored in order to develop efficient clinical stem cell therapies. The cell localization and distribution must be determined in a non-invasive manner. In fact, *in vivo* tracking and localization of these therapeutic agents (stem cells) is one of the main challenges in imaging. The use of nanometre-sized superparamagnetic iron oxide or metal-doped iron oxides allows a non-invasive detection to identify and follow the cell fate by magnetic resonance imaging (MRI). Superparamagnetic nanoparticles are the preferred magnetic label for MRI due to its biocompatibility and strong effects into transverse relaxation.

Our laboratory has great experience in preparing gold nanoclusters and semiconductor nanocrystals functionalized with different types of carbohydrates (glyconanoparticles) [1]. We have recently prepared biofunctional high quality magnetic core-shell Fe_3O_4@Au nanoparticles with the appropriate size, shell and water solubility to further bioconjugate to the specific antibody. Between the different approaches to attach antibodies, we have chosen the covalent immobilization of protein G. This protein selectively and non-covalently immobilizes the Fc regions of IgG from diverse mammals constituting a promising anchoring platform to capture oriented antibodies. In this procedure a potential loss of antibody activity is avoided.

On the other hand the group in CIB-CSIC have generated monoclonal antibodies (NILO) against neural stem cells (NSC) which identify and define a specific brain area, the subventricular region (SVZ) [2]. These cells can be expanded “in vitro” as neurospheres, differentiate to neural lineages (oligodendrocytes, astrocytes or neurones) and can regenerate demyelinating damaged tissue. The introduction of this specific antibody conjugated to magnetic nanoparticles will permit an efficient labelling due to its specific binding properties against a cell subpopulation in the neurospheres.

We have prepared magnetic coated iron oxides nanoparticles conjugated to protein G and the specific antibody Nilo 2. The construction Fe3O4-Au-Prot G-Nilo2 has been characterized and for their application as MRI contrast agents to label NSC in vivo. The longitudinal and transversal relaxation times (T_1 and T_2) of our MGNPs were measured.
Our first biological study consists of in vitro incubation of neurospheres with our MGNPs functionalized with Nilo 2. The labelling was characterized by flow citrometry and fluorescence microscopy. Our magnetic structures label a subpopulation of cells growing as neurospheres when they were incubated with MGNP coupled with Nilo 2 antibody. Preliminary in vivo experiments have been made in healthy and cerebral damaged mice.

References:

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[2] Del Valle I., Garcia-Benzaquen L., Kremmer L., Martinez S., Silva A. Identifying mouse neural stem cells with monoclonal antibodies able to arrest neurosphere proliferation and differentiation (in preparation).